

Nanotechnology: Regulatory Challenges

Presented By:

Phillip M. Buckler

Vice President of Regulatory Affairs and Quality

Kereos, Inc.

St. Louis, MO

Presented at the FDA Nanotechnology Open Meeting

October 10, 2006

Bethesda, MD

Definition of Nanotechnologies

- Size
 - $\leq 100\text{nm}$
- Differential performance
 - Components organized on a nanometer-scale have significantly better/different performance than on a larger-scale

Diversity of Nanotechnologies

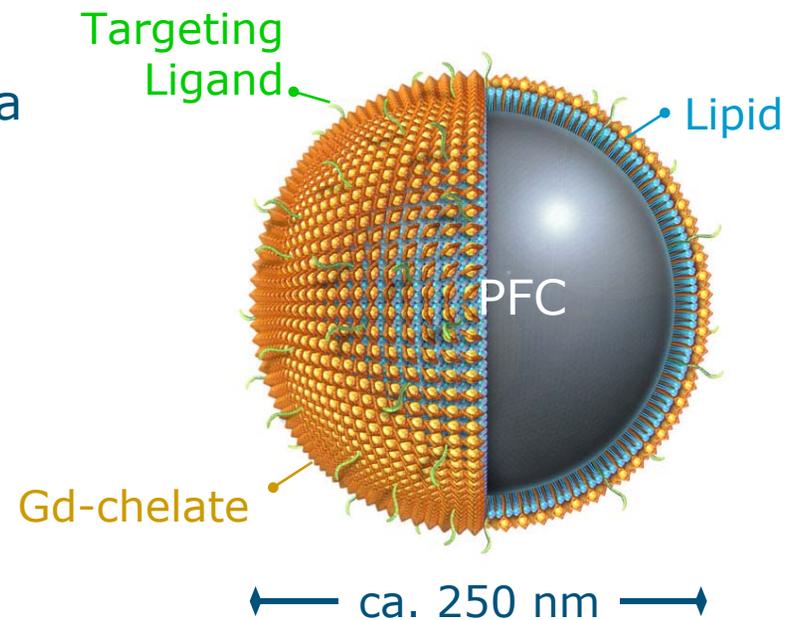
- MEMS/NEMS
- Nanocrystals
 - API milling
 - Quantum Dots (CdSe)
- Nanotubes/Buckyballs (C_x)
- Nanowires
- Nanoparticles (metal, protein, etc.)
- Nanodroplets (micelles, PFC emulsions, etc.)

Nanotech Safety Framework

- Non-nanotech composition
 - Safety, distribution of constituents in bulk
 - Existing drug/device guidance
- Nano-structure impact
 - Novel activity/reactivity
 - Biodistribution
 - Bioavailability

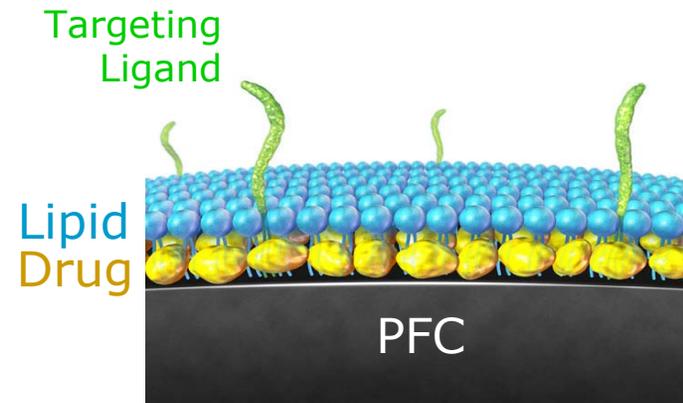
Example: Kereos LTEs

- Ligand-Targeted Emulsions
 - “Oil-in-water” emulsions
 - Specific
 - + Ligand “targets” the disease
 - + Delivers payload to specific area
 - MRI: paramagnetic ion chelate
 - Therapeutic: paclitaxel
 - + 10-100 ligands
 - + $\approx 100,000$ payload molecules



Example: Kereos LTEs

- Kereos “oil-in-water” emulsions
 - Specific
 - + Ligand “targets” the disease
 - + Delivers payload to specific area
 - MRI: paramagnetic ion chelate
 - Therapeutic: paclitaxel
 - + 10-100 ligands
 - + $\approx 100,000$ payload molecules



Example: Kereos LTEs

- Non-nanotech composition
 - Safety, distribution of constituents in bulk
 - Liquid perfluorocarbon
 - + Well-understood human safety as parenteral at higher doses
 - Paclitaxel
 - + Extensive human safety experience, etc. as parenteral at higher doses
 - Gadolinium chelate
 - + Several approved agents at much higher doses
 - Targeting ligand
 - + NCE, small molecule RGD peptidomimetic

Example: Kereos LTEs

- Non-nanotech composition
 - Existing drug/device guidance
 - + Liposome guidance
 - + Imaging guidance (3) (MRI agent)
 - + Other guidance (therapeutic)
 - Non-clinical
 - Combination products

Example: Kereos LTEs

- Nano-structure impact
 - Novel activity/reactivity
 - Biodistribution
 - + Impact of targeting on PFOB and “payload” distribution
 - + Differential clearance of Gd-chelate or paclitaxel vs. non-LTE
 - Bioavailability

Conclusions

- Nanotechnology – broad umbrella
 - More useful as a word than as a classification
 - Argues against one-size-fits-all approach
- Safety considerations should be based on
 - Non-nanotech composition
 - + Safety/toxicity of components
 - + Appropriate existing drug/device guidance
 - Changes due to nanostructure